REMARKS

Claims 11, 12, 16-18, 22-24, 29-31 and 33-37 are pending in the application. Claims 1-10, 13-15, 19-21, 25-28 and 32 have been cancelled. Claims 11, 12, 16-18, 22, 24 and 29-31 are amended herein. New claims 33-37 have been added. Support for the amendments to claims 11, 12, 16-18, 22, 24 and 29-31 and for new claims 33-37 may be found at least on page, 6, lines 13-18, page 11, final paragraph an original claims 16-18. No new matter has been added with the amendments and new claims. Entry and consideration thereof are respectfully requested.

Rejections under 35 U.S.C.§112, 1st paragraph - enablement

The Examiner maintains the rejection of claims 11-18, 22-24 and 28-29 with the assertion that the specification is not enabled for nucleic acid molecules sharing 50% sequence identity with SEQ ID NO:1 encoding an antimicrobial protein. In the Office Action the Examiner cites the "Wands Factors" in rejecting the claims for lack of enablement. Each of the Wands Factors is addressed as appropriate below.

1) Nature of the Invention: The invention, as most broadly encompassed by the amended claims, is directed to nucleic acids encoding antimicrobial proteins having pyranose oxidase activity and having 80-100% identity with SEQ ID NO:1.

2) Breath of the claims: The Examiner notes in part that "Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these region can tolerate only conservative substitutions or none at all." Applicants note that claims have been amended to recite a minimum sequence identity of 80%. Thus, at most 20% of the sequence can be altered, compared to ½ of the sequence as previously recited. In addition, new claims 35-37 recite the additional feature that the changes in the sequence are through conservative substitutions of amino acids.

3) Predictability of the art: The Examiner indicates that DNA protein sequence arts are "unpredictable". In support of this position the Examiner cites to Lazar et al. (1988). The Examiner also cites to a reference disclosing a protein having 53.3% identity that has a completely different function from the proteins of the present invention.

Applicants first note that the reference cited by the Examiner for the general proposition of unpredictability in the field was published more than 10 years prior to the earliest priority date of the present invention. The field of nucleic acids and proteins was effectively a completely different world in 1988 than it was at the time of the invention (1999), due to technological developments. This is evidenced by the fact that a search of the

USPTO patent database with the search term "DNA" yields approximately 70,000 U.S. patents. Of those 70,000 patents, less than 5,000 were filed or issued as of 1988, the publication date of the reference relied by the Examiner. In comparison, approximately 35,000 patents were filed or issued between 1988 and 1999 that somehow relate to "DNA." This reflects a nearly exponential growth in the field. Similarly a search of the USPTO patent database with the term "protein" yield approximately 125,000 hits, of which approximately 25,000 were filed or issued as of 1988, whereas approximately 60,000 were filed or issued between 1988 and 1999, reflecting a 2 ½-fold growth in the rate of development in this area. In addition, because technology builds upon itself, the advances by 1999 are not equal to the advance of 1988. As such, a reference dating from 1988 is not indicative of the state of the art or predictability of the art in 1999.

With regard to the reference of Kawamura et al., Applicants note that the claims have been amended to recite at least 80% identity. Thus, this reference is no longer relevant.

4) Amount of direction or guidance provided: The Examiner asserts that the specification fails to provide guidance as to which domains are important in the protein to maintain antimicrobial activity. The Examiner further notes that the claims

recite "gene" however genes require introns and exons. The claims have been amended to recite a minimum of 80% sequence identity. The claims have been further amended to recite that the encoded protein has pyranose oxidase activity. It would be routine to generate sequences having at least 80% sequence identity and test the encoded protein for pyranose oxidase activity based on commonly known techniques and the disclosure of the specification. In addition, with regard to recitation of the term "gene", the claims have been amended to recite "nucleic acid". This amendment is supported by at least the Examples of the specification.

5) The presence or absence of working examples: The Examiner notes that the specification provides examples of 65 and 70kDa proteins of SEQ ID NOS:3-6, having pyranose oxidase activity. The Examiner further notes that the specification provides examples of how the cDNA encoding the protein was identified. The Examiner asserts that the specification fails to provide examples of which regions, domains or sequences are important to maintain biological activity. The Examiner again cites to Lazar (1988) in support of this position.

As discussed above, the claims have been amended to further define the invention as requiring at least 80% sequence identity. In addition, the claims have been amended to recite that the

encoded protein has pyranose oxidase activity, which may be tested for as disclosed in the specification. Finally, as discussed above, Lazar (1988) is not indicative of the state of the art at the time of the invention or of the guidance that would need to be provided by the working examples to practice the invention.

6) Quantity of experimentation necessary: The Examiner indicates that, "given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required...."

Each of the issues relied upon for the position that undue experimentation would be required have been addressed above. Regarding the breath of the claims, the claims have been amended to require at least 80% sequence identity and that the protein has pyranose oxidase activity. Regarding the predictability and guidance, this issue has been addressed by the amendments to the claims. In addition, the reference relied upon the Examiner of Lazar (1988) is not indicative of the art in 1999.

7-8) State of the prior art and the relative skill of those skilled in the art, respectively: These considerations have been addressed by the preceding comments under 1-6), above.

In the rejection the Examiner further indicates on page 6 that the function of a protein with only 50% homology/identity cannot be predicted and that the specification fails to provide sufficient guidance regarding the domains of the protein to be predictive of activity. In addition, the Examiner asserts that claim 12 broadens the breath of the claims by reciting a sequence that hybridizes to a sequence having 50% homology with SEQ ID NO:1 at low stringency conditions of 45° C.

In view of the Examiner's remarks the claims have been amended to further define the invention with the features that the gene encodes an antimicrobial protein having pyranose oxidase activity. Support for this amendment may be found at least on page 39, Table 2 and cancelled claim 28. Claim 11 (and dependent claims 12, 16, 22, and 35 further recite the feature that the sequence has 80% or more identity. Dependent claims 17 (and 33 and 36), 18 (and 37) further define the sequence identity as being at least 90% or 95%, respectively.

Regarding the assertion that claim 12 expands the breath of the claims, applicants believe that the intent of the claim may have been misunderstood. Claim 12 recites a nucleic acid which is complementary to a base sequence, that hybridizes to SEQ ID NO:1 under stringent conditions. Thus, claim 12 encompasses only

sequences that hybridize to SEQ ID NO:1, not sequences which hybridize to sequences having 50% homology to SEQ ID NO:1.

In addition, claim 12 recites, "high stringency". Thus, even if 45°C is used as the hybridization temperature, other hybridization conditions must be used to that maintain high stringency. Finally, claims 12, 29, and 31 have been amended to recite hybridization conditions of "6XSSC, 68°C (without formamide)". In this regard, reference is made to the "WRITTEN DESCRIPTION GUIDELINE TRAINING MANUAL" issued on March 2000, by the USPTO. In Example 9, Hybridization of the TRAINING MANUAL, a claim for a nucleic acid that specifically recites hybridization under highly stringent conditions (6XSSC and 65°C) is recognized as meeting the written description requirement. The hybridization conditions of amended claim 12 are more stringent, i.e. with 68°C, than the hybridization conditions exemplified in Example 9 of the manual.

In summary, the present claims have been amended to significantly restrict the scope of the invention from the claims as rejected by the Examiner. For example, claim 11 has been amended to restrict the sequence identity from 50% to 80% amino acid sequence identity of SEQ ID NO:2. In addition, claim 12, as well as the other claims reciting hybridization conditions have been limited to 6XSSC, 68°C (without formamide), i.e. hybridization

conditions which would encompass only sequences of very high homology to the specific recited SEQ ID NO. For the above-discussed reasons, the claims as currently pending are fully enabled. Reconsideration of the amended claims and withdrawal of the rejection is therefore respectfully requested.

Applicants further note, as discussed above, that new claims 35-37 further define that the identity is made through the conservative substitution of amino acids, i.e. wherein the substitution of one or more amino acids of SEQ ID NO:2 is by replaing a hydrophobic amino acid with a hydrophobic amino acid, a hydrophilic amino acid with a hydrophilic amino acid, an acidic amino acid with an acidic amino acid or a basic amino acid for a basic amino acid. One skilled in the art readily would readily be able to obtain nucleic acids of the invention wherein there is at least 80% sequence identity and the differences in the sequences is through the conservative substitution of amino acid residues. In addition, one skilled in the art would fully expect such a nucleic acid to in most instances encode a protein having the functional activity as defined in the claims.

Objections to the claims

Claim 12 has been objected to for being improperly dependent and failing to further limit the subject matter of the previous claim. The Examiner indicates that claim 12 expands the scope of claim 11 by reciting conditions of low stringency. Applicnts believe that this objection is based on the misunderstanding of claim 12 as discussed above.

In addition, claim 12 has been amended to define the temperature of hybridization as 68°C. Withdrawal of the objection is respectfully requested.

Rejections under 35 U.S.C.§112, 1st paragraph - written description

Claims 29-31 have been rejected under 35 U.S.C.§112, 1st paragraph for lack of written description. More specifically, claims 29-31 have been rejected for encompassing a genus not adequately described in the specification because of the broad temperature range of hybridization recited in the claims. The claims have been amended to define the temperature of hybridization as 68°C, thus deleting conditions of the low stringency from the claims. As discussed above, the hybridization conditions now recited in the claims are more stringent than those indicated in the USPTO TRAINING MANUAL exemplified for meeting the written description requirements.

Applicants note that the Examiner also includes claim 30 in the rejection. However, claim 30 is an independent claim that does not recite hybridization conditions. As such, it is believed that the inclusion of claim 30 in the rejection was in error. In addition claim 31, recites all of the features of claim 30, plus additional features. As such, claim 31 should similarly not be included in the rejection.

For the above discussed reasons, withdrawal of the rejection is respectfully requested.

Claim 24 has been rejected for being drawn to the overly broad genus of any transformed organism. Claim 24 has been amended to be drawn to a "transformed microorganism". Support for this amendment may be found at least in the working examples of the specification. Withdrawal of the rejection is therefore respectfully requested.

Rejections under 35 U.S.C.§112, 2nd paragraph

Claims 11-20, 22-24, 28 and 32 have been rejected under 35 U.S.C.§112, 2nd paragraph as being unclear. More specifically, claim 11 has been rejected with the assertion that it not clear how the peptides are to be combined. Claim 11 has been amended to delete recitation of "or a combination of these polypeptides." Withdrawal of the rejection is respectfully requested.

Claims 19, 20 and 32 have been rejected for being indefinite in being drawn to the use of two domain sequences for determination of the sequence. Claims 19, 20 and 32 have been cancelled, thus rendering this rejection moot.

Rejections under 35 U.S.C.§102(e)

Claims 19 and 32 have been rejected under 35 U.S.C.§102(e)as being anticipated by US '294. Claims 19 and 32 have been cancelled, thus rendering this rejection moot.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD (Reg. No. 40,069) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. 1.17 and 1.136(a), the Applicants respectfully petition for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $420.00 is attached.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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